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## DOES LAYER 4 IN THE BARREL CORTEX FUNCTION AS A BALANCED CIRCUIT WHEN RESPONDING TO WHISKER MOVEMENTS?

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**Abstract**—Neurons in one barrel in layer 4 (L4) in the mouse vibrissa somatosensory cortex are innervated mostly by neurons from the VPM nucleus and by other neurons within the same barrel. During quiet wakefulness or whisking in air, thalamic inputs vary slowly in time, and excitatory neurons rarely fire. A barrel in L4 contains a modest amount of neurons; the synaptic conductances are not very strong and connections are not sparse. Are the dynamical properties of the L4 circuit similar to those expected from fluctuation-dominated, balanced networks observed for large, strongly coupled and sparse cortical circuits? To resolve this question, we analyze a network of 150 inhibitory parvalbumin-expressing fast-spiking inhibitory interneurons innervated by the VPM thalamus with random connectivity, without or with 1600 low-firing excitatory neurons. Above threshold, the population-average firing rate of inhibitory cortical neurons increases linearly with the thalamic firing rate. The coefficient of variation CV is somewhat less than 1. Moderate levels of synchrony are induced by converging VPM inputs and by inhibitory interaction among neurons. The strengths of excitatory and inhibitory currents during whisking are about three times larger than threshold. We identify values of numbers of presynaptic neurons, synaptic delays between inhibitory neurons, and electrical coupling within the experimentally plausible ranges for which spike synchrony levels are low. Heterogeneity in in-degrees increases the width of the firing rate distribution to the experimentally observed value. We conclude that an L4 circuit in the low-synchrony regime exhibits qualitative dynamical properties similar to those of balanced networks.

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**Key words:** layer 4, barrel, inhibitory neurons, balanced state, theory, model, synchrony.

### INTRODUCTION

The lemniscal pathway in the whisker somatosensory system of rodents conveys information about whisker movement and touch (Yu et al., 2006; Diamond et al., 2008). Mechanosensory neurons in the trigeminal ganglion convert the forces and moments resulting from whisker bending into neuronal signals (Bush et al., 2016; Campagner et al., 2016). These signals flow through the trigeminal nuclei in the brainstem to the VPM thalamic nucleus and then to layer 4 (L4) in the primary somatosensory cortex (S1) (Ahissar et al., 2000). Information from a specific whisker is primarily conveyed to a corresponding barreloid in the VPM, and that barreloid primarily projects to a corresponding barrel in L4 in S1 (Meyer et al., 2013). Excitatory (L4E) neurons and inhibitory (L4I) fast-spiking, parvalbumin (PV)-expressing neurons in a barrel are mostly connected to other L4E and L4I neurons in the same barrel, and only sparsely to L4E and L4I neurons in neighboring barrels (Hooks et al., 2011). VPM thalamus provides the only known source of long-range input to L4 barrels, except for neuromodulation (Lefort et al., 2009; Ma et al., 2012). Therefore, as a first approximation, an L4 barrel can be viewed as an isolated and localized neuronal circuit. Such a system is ideal for examining the interplay between the dynamics of the circuit and its ability to process sensory information. This examination can be carried out using various experimental techniques together with theoretical and modeling studies.

The number of neurons in a barrel varies across rodent species. In the mouse, there are about 200 neurons in the C2 barreloid in the VPM and about 1600 excitatory neurons in the C2 barrel in L4 (Lefort et al., 2009). Interneurons in cortex comprise 15–20% of all cortical neurons (Gabbott and Somogyi, 1986; DeFelipe and Farinas, 1992; Beaulieu, 1993; Tamamaki et al., 2003), of which about half are PV neurons (Lee et al., 2010). There are therefore about 150 PV neurons in that barrel. The synaptic connection probability between two PV neurons is 0.4–0.5 (Ma et al., 2012; Karnani et al., 2016). During states of quiet wakefulness (no whisking) or whisking without touch, VPM and PV neurons in L4 fire at average rates on the order of 10 Hz, whereas L4 excitatory neurons rarely fire (Hires et al., 2015; Yu et al., 2016). Somatostatin (SOM)-expressing inhibitory interneurons only rarely receive VPM input (Beierlein et al., 2003), and there is no indication they receive rapid trains of action potentials from excitatory neurons that are needed to activate them (Kapfer et al., 2007; Silberberg and

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Markram, 2007). Therefore, as a first approximation, the circuit can be viewed as a network of ~150 interconnected L4I neurons innervated by ~200 VPM neurons.

Theoretical investigations of cortical networks have mostly focused on networks with large numbers of neurons and synaptic connections. The “de facto standard model” (Latham, 2017) of large networks of spiking neurons was developed by (van Vreeswijk and Sompolinsky, 1996, 1998). The model was developed under the following assumptions: 1. The network is composed of large populations of excitatory and inhibitory neurons. 2. Each neuron is innervated by large numbers of excitatory and inhibitory connections. 3. The synaptic coupling between neurons is sparse and random. 4. The total excitatory and inhibitory synaptic conductance a neuron receives is large. Under these assumptions, and if the firing patterns of neurons in the network are asynchronous (Renart et al., 2010), the total excitatory current and the total inhibitory current a neuron receives are much larger than the current threshold for spiking. The circuit can reach a state in which the population-average firing rates of the excitatory and inhibitory population are neither very large (“epileptic-like”) nor zero only if excitation and inhibition balance each other (“balanced state”), such that the fluctuation and the average of the algebraic sum of the input currents to a neuron are similar in magnitude. As a result, the average firing responses of excitatory and inhibitory populations are proportional to the external input strength. The average coefficient of variation (CV) is on the order of 1, and increases with the strength of the total conductance (Lerchner et al., 2006).

The numbers of neurons and synaptic connections in the L4 barrel circuit are moderate, and the network is not sparsely connected. Despite these facts, do the dynamics of the L4 circuit in the barrel cortex of mice behave as would be predicted from balanced-state models? To address this issue, we construct a circuit model composed of spiking neurons based on the known anatomy and physiology of the L4 circuit, and explore whether it functions dynamically as expected from a balanced network.

## THE MODEL

We consider a model of an interconnected network of PV interneurons in layer 4, termed L4I neurons and denoted by the  $I$  superscript. The neurons are innervated by excitatory VPM thalamic (T) neurons. P<sub>Om</sub> thalamic input is not included into the model because P<sub>Om</sub> neurons rarely project to excitatory and PV inhibitory neurons in barrels in L4 of the primary somatosensory cortex (e.g., Fig. 3B in (Hooks, 2017); (Koralek et al., 1988; Lu and Lin, 1993; Ahissar et al., 2000; Bureau et al., 2006)). The thalamic signals from each VPM neuron are modulated according to the whisking phase and the preferred phase of the neuron. The population-average VPM firing activity is slowly modulated in time, such as during non-whisking or whisking in air (Yu et al., 2016). L4 excitatory neurons fire sparsely (the average firing rate is ~0.5 Hz; Yu et al., 2016) during these states, and, as a first step, are not taken into account in

the model. Their additional excitatory currents applied on PV inhibitory neurons are approximated by elevating the firing rates of VPM neurons. The effects of approximating excitation from L4E neurons by considering VPM neurons firing at higher rates are estimated at end of the Results section. Other types of inhibitory interneurons include SOM neurons that do not receive VPM inputs (Beierlein et al., 2003), and VIP neurons that mostly inhibit SOM neurons (Karnani et al., 2016). Their firing patterns during whisking states have only recently started to be investigated (Munoz et al., 2017), and they are not considered here.

## SINGLE CONDUCTANCE-BASED L4I NEURON MODEL

Following previous work on cortical dynamics (Wang and Buzsaki, 1996; Hansel and van Vreeswijk, 2012), single L4I neurons are governed by a modified Wang-Buzsáki model (Wang and Buzsaki, 1996) with one compartment. The membrane potential  $V_i^j$  where  $i = 1, \dots, N_i$ , obeys

$$C \frac{dV_i^j}{dt} = -I_{L,i}^j - I_{Na,i}^j - I_{Kdr,i}^j - I_{syn,i}^j - I_{el,i}^j \quad (1)$$

where  $C$  is the neuron capacitance,

$$I_{L,i}^j = g_L (V_i^j - V_L) \quad (2)$$

is the leak current, the conductance of the leak current is  $g_L = 0.1$  mS/cm<sup>2</sup>,  $V_L = -65$  mV and  $C = 1$  μF/cm<sup>2</sup>. The currents  $I_{syn,i}^j$  and  $I_{el,i}^j$  are the total input currents from chemical and electrical synapses respectively. The other ionic currents are:  $I_{Na}^j = g_{Na} m_{\infty}^3 h (V - V_{Na})$ , where  $m_{\infty} = \alpha_m(V) / (\alpha_m(V) + \beta_m(V))$ , and  $I_{Kdr}^j = g_{Kdr} n^4 (V - V_K)$ . The kinetics of  $h$  and  $n$  are given by

$$dh/dt = \phi [\alpha_h(V)(1-h) - \beta_h(V)h], \quad dn/dt = \phi [\alpha_n(V)(1-n) - \beta_n(V)n] \quad (3)$$

The functions  $\alpha(V)$  and  $\beta(V)$ , for  $V$  in mV, are:  $\alpha_m(V) = 0.1(V+30) / \{1 - \exp[-0.1(V+30)]\}$ ,  $\beta_m(V) = 4 \exp[-(V+55)/18]$ ,  $\alpha_h(V) = 0.7 \exp[-(V+44)/20]$ ,  $\beta_h(V) = 10 / \{1 + \exp[-0.1(V+14)]\}$ ,  $\alpha_n(V) = 0.1(V+34) / \{1 - \exp[-0.1(V+34)]\}$ ,  $\beta_n(V) = 1.25 \exp[-(V+44)/80]$ ,  $\phi = 0.2$ . The parameters of the model are:  $g_{Na} = 100$  mS/cm<sup>2</sup>,  $V_{Na} = 55$  mV,  $g_{Kdr} = 40$  mS/cm<sup>2</sup>,  $V_K = -90$  mV.

## SINGLE INTEGRATE-AND-FIRE L4I NEURON MODEL

In Fig. 3D, we examine networks of inhibitory integrate-and-fire neurons to explore the role of intrinsic neuronal properties on the circuit dynamics. Eq. (1) is replaced by the following scheme

$$C \frac{dV_i^j}{dt} = -I_{L,i}^j - I_{syn,i}^j \quad (4)$$

When the membrane potential of a neuron reaches the threshold value,  $V_{th} = -54$  mV, it fires a spike, and the membrane potential is reset immediately to  $V_i^j = V_L$ .

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